DISCUSSION

J. F. ANDERSON, M. D. (1930 Wilshire Boulevard, Los Angeles).—I wish to emphasize a few of the points that Doctor Langley has made. In the first place, the importance of not making a diagnosis on an electrocardiogram alone. In some cases it is possible to make a diagnosis on the tracing, and in some it is possible to do so on clinical findings and history. But in either method a grave error may be made. Infections and intoxications may give similar electrocardiographic findings, and symptoms may be misleading. It is by combining the two that by far the best results are obtained. In this case we can often diagnose coronary sclerosis before thrombosis occurs, and by careful management at least postpone a more serious condition. The most valuable findings in the chronic coronary disease are: intraventricular block, as evidenced by widening of the QRS interval beyond .1 second, and bundle-branch block. In the acute cases the earliest and most characteristic finding in the electrocardiogram is displacement of the RT segment. It will take off high on the R in one or two leads, and low on the S in the other lead, or vice versa. This change may be seen in only a few hours after the attack. It is, in turn, followed by the T-wave changes. I think it would be well also to emphasize the fact that the electrocardiographic changes may be slight and may not extend through a long period of time. Thus one normal tracing after an attack, the symptoms of which suggest coronary thrombosis, does not necessarily mean that the patient does not have a coronary occlusion. It is rare indeed, however, that several tracings are negative when the trouble is really present.

There has been much discussion lately about the significance of the large Q-wave in Lead 3. Due to confusion in nomenclature, two main types of complexes are described. In the first place, an inverted R3 (S3) is shown as the large Q, when the application of Einthoven's equation readily identifies it as the former. Thus the tracing shows left-axis deviation, which is significant only if it denotes left ventricular preponderance.

The second type is a diphasic QRS in which the initial phase is directed downward. This variety may become monophasic, however, with respiration, termination of pregnancy, or loss of weight. Occasionally a tracing with normal axis deviation and a large initial downward phase is shown. When found a large Q3 is most frequently seen in cases of coronary disease and left ventricular abnormality. The cause or mechanism of production, however, has not yet been determined. The latest investigators are inclined to the belief that change in the anatomical position of the septum has more to do with its production than deficient blood supply, or myocardial damage.

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WILLIAM DOCK, M. D. (Stanford University Medical School, San Francisco).—There is nothing I can add to Doctor Langley's paper or Doctor Anderson's discussion of the electrocardiographic findings in acute myocardial infarction. It must be emphasized that the string galvanometer is an instrument exactly like the stethoscope in that it extends the examiner's powers of physical examination. Unfortunately it is more expensive than the stethoscope, but in practice it should be used, like the stethoscope, as often as necessary. In cases of typical coronary occlusion it is not necessary to think of the electrocardiogram just as it is not necessary to listen to the heart of a typical case of aortic insufficiency with bobbing neck vessels and a Corrigan pulse. However, most of us still enjoy seeing typical "coronary" tracings or hearing aortic diastolic murmurs. In cases where the diagnosis of coronary disease is doubtful, and where a correct decision is of vital importance, the taking of frequent tracings usually is of great value in furnishing a definite solution of a problem which no other form of physical examination could solve.

ARTHUR STANLEY GRANGER, M. D. (2007 Wilshire Boulevard, Los Angeles).—It will not be amiss to lay a little more stress on one or two points which have been mentioned in Doctor Langley's paper and emphasized by both Doctor Anderson and Doctor Dock in their discussions. We must remember that a very large percentage of patients presenting symptoms of angina pectoris and who, we must assume, have definite coronary disease show absolutely normal electrocardiographic tracings. Many of us have seen such patients turned aside with the diagnosis of either neuritis or neurosis, and at least one or two of them, in my experience, have later died of coronary occlusion. Again, some of the electrocardiographic signs, which are commonly found in coronary disease, may be due to other conditions. Consequently it is essential that we do not rely on the electrocardiograms alone as a means of diagnosis, but try to correlate the electrocardiographic signs with a careful history of the condition together with the physical findings, and in some instances it is necessary to make the diagnosis from the history alone. I am always suspicious of coronary disease in a patient presenting the type of pain which is commonly seen in that condition despite the absence of any positive signs, and in case of doubt it is far better to be mistaken in one's diagnosis than to err in the opposite direction.

ECZEMA—OBSERVATIONS ON DESENSITIZATION*

By PHILIP K. ALLEN, M. D.
San Diego

DISCUSSION *by Ernest D. Chipman, M. D., San Francisco; George Piness, M. D., Los Angeles; Albert H. Rowe, M. D., Oakland.*

THE present-day treatment of eczema or dermatitis eczematosa has been radically influenced by the newer concepts of the pathogenesis of this condition. Recent knowledge on this subject points strongly to the conclusion that eczema is not a metabolic disease, but is in the main an allergic one, in the sense that it represents a reaction of a sensitized group of cells to one or more specific excitants. Although it was long believed that sensitization to protein substances was necessary to the production of allergic reactions, we have learned that a reaction of the epidermis, with the production of clinical eczema, may be precipitated by contact with nonprotein substances which are harmless to the normal individual.

As a matter of fact, wide clinical experience shows that sensitivity to exogenous nonprotein substances is the predominant factor in the specific etiology of adult eczema,[1] and that endogenous proteins, such as foods, play a relatively unimportant rôle.[2] In short, the presence of clinical eczema in an individual is strongly indicative of a specific hypersensitiveness of the epidermal cells to an external excitant. It is not within the scope of this paper to present the proofs of this assertion, and the bald statement will have to be supported by references to the above representative articles from the voluminous literature on the subject.

It was the persistent search for endogenous proteins as a specific etiologic basis for eczema that

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was largely responsible for the early poor success of the allergist and dermatologist working this field.

DIAGNOSIS AND TREATMENT

In the diagnosis, the functional or patch test with suspected external irritants has largely replaced the scratch and intradermal protein tests. This method has proved an invaluable aid in the determination of previously obscure dermatitides.

In the treatment, such nonspecific contributory factors as focal infection, constipation, endocrine disturbances, "nervousness," etc., although treated when present, deserve only secondary consideration. The hope of complete and permanent cure logically lies in discovery of the basic etiology and specific therapy against it. Obviously, specific therapy consists in removal of the excitant or, if this is impracticable, in desensitization against it.

SENSITIZATION

In a discussion of desensitization, its antithesis, sensitization, demands at least brief consideration.

In spite of the uniformity of clinical characteristics in dermatitis eczematosa, etiologic and immunologic findings demand a recognition of two more or less well-defined groups.

The first, and larger, of these includes the cases of "contact dermatitis," formerly known as "dermatitis venenata." This group, of which the eruption caused by poison ivy is typical, represents a reaction of the intact skin to contact with substances usually of nonprotein nature. Sensitization to these substances usually does not result in the formation in the blood stream of demonstrable antibodies.[3] Hypersensitiveness in this group is apparently not subject to hereditary influence as is shown by the fact that a large percentage of individuals may be sensitized by sufficient exposure to an eczematogenous substance and that this percentage varies with the nature of the excitant (orthoform, 45 per cent; ivy, 65 per cent; primrose and nickel salts, 100 per cent).[2] Although individual predisposition probably plays a part in this type of sensitization, the capacity to become specifically sensitized appears to be common to all skins to a greater or less degree.[4] Therefore the production of such a hypersensitiveness seems to depend on one main factor—sufficient exposure to a strongly eczematogenous substance.

The second and smaller group of eczemas is composed of those cases belonging to the asthma-hay fever-eczema complex, variously designated as "allergic state," "atopy," "true allergy," or "primary allergy." They usually represent a hypersensitiveness to foreign proteins, and are subject to a definite hereditary influence.[5, 6] The sharp segregation of this group is demanded by the fact that the blood stream in these individuals regularly contains circulating antibodies specific for the antigen. These antibodies may be demonstrated by the well-known Prausnitz-Küstner method of passive transfer. Bloch states, "Without doubt all forms of idiosyncrasy in which a clear Prausnitz-Küstner reaction is obtained, and are therefore incontestable antigen-antibody reactions, belong to one special group." Since for purposes of discussion a specific term is necessary to differentiate this group, the term "atopy" as suggested by Coca[7] will be used here. The term applies only to those individuals who show predisposition, usually inherited, to protein sensitization and in whom free antibodies can be demonstrated for a specific antigen. Concerning these free antibodies, Coca[8] remarks, "Their constant presence related to the excitant in hay fever, the so-called 'sensitive' group of asthmatics, and in some cases of atopic eczema, point to these bodies as the actual mechanism of the hypersensitiveness." The immediate (wheal) reaction to a protein with the scratch or intradermal test, or the demonstration of specific blood antibodies, is far from conclusive proof that the protein is the direct cause of the eczema. The wheal reaction is not eczema, and represents a reaction of a group of cells different from those concerned in eczema. The existence of such an entity as "atopic eczema" has been seriously doubted by many observers and is still the subject of controversy. However, whether the eczematogenous effect of proteins is a direct or an indirect one, the prevalence of eczema in atopic individuals leaves little doubt that endogenous protein substances may play a part in its production.[6] This is especially true in children.

In attempting desensitization in this atopic group, two very important points must be borne in mind:

1. The individual has a hereditary predisposition to protein sensitization.

2. The presence of circulating antibodies with the possibility of a severe constitutional reaction requires extreme caution in injecting the antigen.

Although eczematous sensitization to silk is not as rare as might be supposed,[9] the following case is unique in many respects. At first glance it seems to fall definitely within the second or "atopic" group.

REPORT OF CASE

A white male, age twenty-two years, presented an itching erythemato-squamous eruption with thickening of the skin, largely confined to the face and flexural surfaces. The upper lip, antecubital fossae, the back of the neck, and a circumscribed area on the wrist showed lichenification and fissuring. The clinical picture was essentially one of "chronic eczema."

There was a definite history of allergic disease on the paternal side. His father had asthma (horse) and eczema. A paternal aunt had asthma, from which she died, and was known to be sensitive to roses.

The patient first experienced eczema during infancy. It disappeared and recurred at irregular intervals until the age of fifteen, when it became severe and refractory to all treatment employed. Since that time the condition had become progressively worse.

Significant in the patient's history was the total absence of any manifestations of asthma, hay fever, or urticaria.

Physical examination disclosed no abnormalities beyond the skin eruption. The laboratory findings were essentially negative.

A large series of contact and percutaneous skin tests with protein and nonprotein substances showed a reaction to only one substance—silk. The reaction to silk was strongly positive with both methods. The response to the patch test was particularly interesting. Irrespective of the silk material used (sized or unsized, dyed or undyed), an erythematous pruritic area would develop within a few hours. Such a contact reaction could not be elicited, however, by prolonged exposure

to silk protein extracts obtained from two different pharmaceutical concerns. The presence in the blood of antibodies specific for silk protein, as contained in these extracts, was shown by repeated passive transfer by the method of Prausnitz-Küstner. The passively sensitized "substitute," however, showed a positive reaction to the scratch and intradermal tests only, and did not react to the patch application.

This patient had realized for some time that contact with silk irritated his skin, and, although he had not associated this fact with the persistence of his eczema, had largely discontinued the wearing of silk clothing. The admonition to avoid all silk clothing and contact with silk resulted in no appreciable clinical improvement.

The fact that only one antigen was discovered is by no means proof of the fact that we were dealing with a monovalent sensitization. Retesting with previously used and additional substances, however, failed to give any other positive reactions. It seemed conceivable that in an individual sensitive to silk, indirect contact with the substance could perpetuate the eruption. As avoidance of such indirect contact seemed impossible, desensitization was undertaken.

An initial desensitizing dose of one minim (.06 cubic centimeter) of a 1:10000 solution of silk protein extract was given subcutaneously. This was followed in twenty minutes by a constitutional reaction together with a marked focal reaction manifested by extreme pruritus and sudden exacerbation of all existing eczematous lesions. An interesting observation was the appearance at this time of urticaria and asthmatic symptoms, conditions of which the patient had never complained.

For two days after the reaction the eczema was markedly improved, the patient stating that his skin was better than at any time during the past five years.

The dosage was greatly reduced, subcutaneous injections being given at four to five-day intervals in gradually increasing amounts. The skin showed definite progressive improvement until a "tolerance level" to injections was reached. This level of tolerance remained remarkably constant, at five to five and one-half minims of a 1:1000 solution of freshly prepared extract. Exceeding this amount invariably resulted in a constitutional reaction, irrespective of how slowly the dose was increased or the time interval between injections.

Although there had been no change in occupation or environment and no local treatment had been given besides cold cream (which he had been using for years), there was marked clinical improvement at this stage. The eruption had entirely disappeared from the majority of areas involved. There remained, however, thickened, somewhat reddened, areas of the upper lip, the neck, and volar surface of the right wrist. There was also occasional itching of these areas. The patch test with silk material to an area of the back which had never been eczematous was now negative after twenty-four hours of exposure. The areas which had previously been involved still reacted to contact with silk, as shown by a localized dermatitis of the patient's face after sleeping on a satin pillow or contact with his wife's silk dress. No change was noted in the capacity of the blood serum to sensitize normal skin.

The inability to produce a higher degree of tolerance after eight months of subcutaneous injections prompted the intradermal administration of the extract. This was suggested by the observation of various investigators who noted better results with this method.

Daily intradermal injections were started with a 1:500 solution of the same extract. Only a minute amount of the solution was given at each injection, which, however, proved sufficient for the production of an immediate wheal reaction. Improvement with this type of therapy was rapid. At the end of four weeks of intradermal injections the entire skin was essentially normal. Itching and erythema had entirely disappeared, and there remained only slight thickening of the skin at the sites of the previous chronic involvement.

The patch test with silk material was now found to be negative in all areas. However, there was still no demonstrable reduction of antibodies as shown by a clear Prausnitz-Küster reaction at this time. There was also no diminution of wheal reaction to intradermal injections of silk protein.

We are forced to the conclusion that the patient has not been desensitized in the strict sense of the word, but is still "atopic." All we have accomplished, evidently, is hyposensitization of the epidermis to the point where it no longer reacts to the usual external contact with the excitant. The therapeutic requirements have been fulfilled, however, in a clinical "cure."

COMMENT

This case presents many interesting features, most of which cannot be discussed here.

Although a specific reaction was obtained to intradermal tests with silk protein extracts, it seems highly probable that some portion of silk material other than the protein itself was the immediate cause of the eczema. The active eczematogenous principle has not as yet been identified, but the reasons for such a conclusion are as follows:

1. The patch test, although positive with silk material, was negative with silk protein extract.
2. Normal skin passively sensitized with antibodies specific for silk protein failed to give a positive reaction to patch tests with silk material.
3. Apparent immunity to contact with silk material has been established in spite of an undiminished antibody reaction to silk antigen.

We have merely demonstrated, therefore, the existence of contact dermatitis in an atopic individual. Although the excitant for both the epidermal and atopic reactions was silk, we have not proved the protein fraction to be the cause of the eruption, nor the existence of such an entity as "atopic eczema."

A parallel example has recently been reported by Brown, Milford, and Coca [10] in a case of hay fever with eczema, both symptoms being due to hypersensitiveness to ragweed pollen. It was definitely established that the protein excitant of the hay fever did not cause the eczema, but that the latter was produced by the nonprotein pollen oil.

This reasoning changes our ideas concerning the specificity of the desensitization with the protein extract. What we had at first presumed to be specific therapy was probably nonspecific for the eczema. Yet this form of treatment was followed by marked clinical improvement.

We have long known that hyposensitization in the human is not analogous to anaphylactic desensitization in lower animals.[11] In the latter, immunity is established by specific neutralization of the antibodies and is readily accomplished. In the human this has been shown not to be the case. Attempted desensitization in atopic individuals does not result in a decrease in the blood antibodies (Coca).

The clinical manifestations of atopy are not due to the mere presence of free antibodies, but demand a hypersensitive or atopic state of the shock organ as well. Since antibodies have been demonstrated in the absence of clinical symptoms,[12] as well as after therapeutic hyposensitization, the beneficial results of treatment in these cases must be attributed to changes in the shock organ.

Whether this altered response of the shock organ is due to a local neutralization of fixed antibodies or to exhaustion of its capacity to react is still an unsettled question.

The apparent advantage of the intradermal over the subcutaneous injections is an interesting one. Sulzberger and Wise [13] recommended this method after successful treatment of a case of ragweed dermatitis. Thommen [14] reports that intradermal injections with pollen extracts in hay fever have proved "decidedly superior" to the subcutaneous method. Phillips [15] reported excellent results with this method and made the interesting observation that the clinical improvement was not dependent upon the amount of antigen injected, but upon the degree of local reaction produced.

A rational explanation of these results is seen in the recent work of Storm van Leeuwen.[16] He has shown that a specific antibody-antigen reaction in the skin reduces the hypersensitiveness to other allergens, and that this nonspecific hyposensitization is directly proportionate to the degree of local reaction produced. This effect was not obtained with wheal reactions to histamin, and the author concludes that the specific reaction has liberated an "intermediary substance," which is an essential factor in hyposensitization. In other words, a substance produced by the interaction of antigen and antibody in the skin is an important element in human hyposensitization.

If this is true, and if epidermal sensitization as encountered in eczema is based on the same mechanism as that of other forms of allergy, we are furnished with an invaluable method of treating eczema in atopic individuals. Further work on this problem is now in progress and will be the basis of a subsequent report.

The immense field opened for this type of therapy is at once obvious. Although the determination of the actual excitant in eczema has been materially aided by the use of the patch test, there still remains a fair percentage of cases in which the exciting substance eludes detection or, if found, cannot be removed.

Specific desensitization has, on the whole, been particularly disappointing in eczema. This may be due, as Bloch suggests, to the tenacity with which the antibody is fixed to the epidermal cell. However, if a prime factor in the process of hyposensitization is the formation of an intermediary desensitizing substance, it is readily seen that the uncomplicated case of contact dermatitis is denied the benefits of this mechanism. It is generally agreed that specific blood antibodies are usually not produced for nonprotein eczematogenous substances. The extract of poison ivy or poison oak may, therefore, be injected subcutaneously or intradermally without the production (except in rare cases) of a constitutional or local reaction.

Theoretically, therefore, such nonspecific hyposensitization of the epidermis requires the existence of an atopic terrain. In such an individual the determination and intradermal injection of a specific atopen should have a nonspecific desensitizing effect on the epidermis irrespective of the nature of the excitant.

I believe that the results obtained in the case reported are far better than those usually seen in attempted specific desensitization in eczema. Since the treatment used was probably nonspecific for the epidermal hypersensitiveness, the explanation of these results may lie in some such mechanism as outlined.

SUMMARY

A case of intractable eczema due to silk is reported in which circulating antibodies specific for silk protein were demonstrated.

The identity of the silk atopen and the skin irritant seems highly improbable.

Injections of silk protein extract (although probably nonspecific for the eczema) were followed by clinical "cure."

Intradermal injections with the production of a local reaction seemed to be more effective than those given subcutaneously.

Such therapy may prove valuable in the nonspecific treatment of eczema occurring in atopic individuals.

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DISCUSSION

ERNEST D. CHIPMAN, M. D. (2000 Van Ness Avenue, San Francisco).—Doctor Allen's paper opens a wide field for discussion which may follow specific or general lines.

Specifically we have to deal with a patient who had an intractable eczema, who reacted to silk when the patch test was employed, but in whom patch tests with silk protein extract were negative. This patient,

however, was cured by the injection of silk protein extract.

It is intimated that these injections were nonspecific for the eczema, and reference is made to the work of Storm van Leeuwen in which it was shown that a specific antibody-antigen reaction in the skin reduces the hypersensitiveness to other allergens.

This case report is of value because it emphasizes the fact that not all allergic reactions are of protein origin and especially because it opens up to our imagination valuable therapeutic possibilities through nonspecific hyposensitization.

In a general sense this paper is of value because of its forthright position in the etiology of eczema. The statement that "sensitivity to exogenous nonprotein substances is the paramount factor in the etiology of adult eczema and that endogenous proteins, such as foods, play a relatively unimportant rôle" should be carefully taken to heart by all of us.

Tradition is tenacious and we part with our deeply rooted notions only after violent struggles. May we ever put over the concept of an eczema that is not even remotely related to the ultimate fate of the protein molecule? May we ever convince the followers of high and holy tradition that because shrimps cause hives in one person no subject of skin disease may eat food from the salt sea? May we ever establish faith in the principle that when dealing with a dermatitis of unknown origin we shall spend our time to better advantage in searching external contacts than in ordering starvation diets or multiple laboratory tests?

If one feels pessimistic about eczema let him ponder over the implications of this paper and be of good cheer.

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George Piness, M. D. (1136 West Sixth Street, Los Angeles).—There is one statement of Doctor Allen's to which exception must be taken unless it be modified and that is, "Wide clinical experience shows that sensitivity to exogenous nonprotein substances is the predominant factor in the specific etiology of adult eczema, and that endogenous proteins, such as foods, play a relatively unimportant rôle." In the first place, it must be emphasized that Doctor Allen speaks of adult eczema, thereby intimating that his statements do not apply to infantile eczema and that adult eczema always differs from infantile eczema in its etiology. This is too broad a statement to leave unchallenged, for many cases of adult eczema undoubtedly belong to the same type or group as infantile eczema and are due to the reaction of endogenous proteins on an allergic individual. Undoubtedly a goodly number of adult eczemas, so-called, are due to contact with exogenous substances, but overemphasis of this fact would leave undiagnosed many cases which can only be recognized by the use of protein skin tests.

The diagnosis of eczema or dermatitis should be made before testing is done, and can be made from the clinical history and character of the lesion. The etiology may then be determined by means of skin testing as Doctor Allen discussed fully in his paper. In our experience all methods are valuable, but one must not be too dogmatic in advising any single one of these methods as being the best. Each of them has a definite place. In the dermatitis due to nonprotein substances we advocate the patch test, and suggest its use also in the forms of dermatitis due to local contact with substances of protein nature, such as is seen on hands of cosmeticians working with orris root, henna, bran; the grocer who handles cereals, etc.; and many other occupational types, as baker, housewife, etc. But our experience over a period of years has taught us that the endogenous group rarely react by the patch test; instead, however, they give excellent and characteristic reactions by the scratch or intracutaneous methods of testing. Again I wish to reiterate that one must not become overenthusiastic over a single method; all of them are valuable aids in assisting us in determining the etiology of dermatitis or eczema when used on properly selected cases.

The case reported by Doctor Allen is not uncommonly seen in a large allergic clinic, and it is to be expected with such a history that the individual should react to silk by any method of testing. In other words, given a sensitive individual tested with a specific protein to which he is sensitive a positive skin reaction will result.

Treatment with specific antigens gives excellent results in most cases of dermatitis due to protein sensitivity, provided proper dosage is given at intervals sufficiently far enough apart to avoid constitutional reactions. The case reported obtained excellent clinical results which may be permanent. However, one must not be too optimistic as it is possible that the individual's tolerance may be broken down again in the future.

The point brought to our attention in this case was the absence of respiratory allergic symptoms. This is characteristic of the allergic dermatitis of the contact type.

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Albert H. Rowe, M. D. (242 Moss Avenue, Oakland).—The relative importance of exogenous as compared with endogenous proteins in the eczema of adults is reversed in infancy as Doctor Allen has mentioned, since most eczema in the first years of life is due to food allergy. My experience, however, still emphasizes the importance of considering ingestants as a cause of eczema in adults and consequently points to the advisability of routine scratch tests followed by intradermal tests with all types of inhalants and foods which have failed to react by the scratch test. Diet trial is also of great value in negative reactors in the diagnosis of food allergy and to determine the true significance of positive food tests. Eczema due to food allergy may be localized and suggestive of contact allergy as exemplified by such eczema, due to wheat, milk, and eggs, of several years' duration on the face of a woman. This patient, moreover, failed to react to these food allergens, and her diagnosis was made through diet trial with elimination diets. The necessity of recognizing food allergy in dermatitis in all ages has been stressed in Urbach's recent book.

But eczema in adults is most frequently due to contact or air-borne substances which can frequently be shown by routine scratch and intradermal reactions. Thus, a woman with a dermatitis all over the face, previously diagnosed lupus erythematosus, reacted intradermally to rose pollen. When she stopped burying her face in roses, which were constantly in her rooms, and received desensitization therapy to rose pollen, she was relieved. Many patients in youth and adult life have dermatitis on the face, neck, arms, and legs due to pollen allergy which can be demonstrated by skin tests.

The patch test should be freely used in the problems of dermatitis. When history suggests definite or unusual contact etiology, it may be used alone without resort to scratch or intradermal tests. Patch-testing should be persisted in with all substances with which the patient has any contact, especially if the other skin tests have not reacted or if such reactions fail to explain the difficulty. The foliage of shrubs, weeds, trees or flowers, and not their pollens, frequently cause eczema only demonstrable with patch-testing. A host of substances such as dyes, drugs, cosmetics, materials used as clothing or furnishings, soaps and occupational substances only react through patch-testing. As Doctor Allen points out, the main requisite for sensitization is sufficiently prolonged contact with such a substance.

Doctor Allen's discussion of his interesting case of silk dermatitis is worthy of study, and his success with intradermal treatment is stimulating to thought. I feel that subcutaneous therapy according to the accepted methods of administration of air-borne allergens might have been carried up to a higher dosage with continued therapy and that the same result, possibly more lasting, might thereby have been obtained. However, the value of intradermal therapy in contact dermatitis must receive more consideration in the future, especially in view of the author's suggestion that it may be nonspecific in part of its activity.

DOCTOR ALLEN (Closing).—I certainly do not wish to imply that protein hypersensitiveness can be ignored as a cause of eczema. The wheal reaction to the scratch or intradermal protein tests is not eczema and does not constitute conclusive proof of the eczematogenous effect of a substance. But it is unquestionable that an allergic reaction to proteins plays an important part in the production of some cases of eczema. Irrespective of whether the effect of such protein sensitization is a direct or an indirect one, it should be given full consideration in the approach to a case.

The point I wished to stress was the relative importance of external contactants in the production of adult eczema. As Doctor Piness has pointed out, I have used the qualifying term "adult" because I believe this type usually represents a different etiology from that concerned in infantile eczema.

True "atopy" seems to be an inherited characteristic and allergic symptoms may appear at birth or shortly afterward. Epidermal sensitivity to contact excitants, however, requires repeated exposure (frequently years) for its production. Therefore this type of reaction is seldom seen in infants. On the other hand, eczematous reaction to endogenous proteins as seen in infantile eczema tends to compensate spontaneously and usually disappears in childhood. Some individuals, it is true, carry an infantile eczema into adult life without remission, and cases of adult eczema have been reported so highly sensitive to a food that the ingestion of a minute amount would cause an eruption.

In the main, however, recent studies have given more and more importance to contact excitants in adult eczema at the expense of endogenous proteins.

X-RAY ASPECTS OF FUNCTIONAL DISORDERS OF THE COLON*

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San Francisco

DISCUSSION *by R. G. Taylor, M. D., Los Angeles; Carl B. Bowen, M. D., Oakland; Charles M. Richards, M. D., San Jose.*

MOST writers on irritable colon emphasize the importance of the nervous element in its causation, and any extended experience with these patients confirms that impression. The nerve supply to the descending colon and sigmoid, which are the segments commonly affected, is intimately related to that of the pelvic organs, and both sympathetic and craniosacral fibers are distributed throughout the colon. The internal sphincter and adjacent colon are innervated from thoracolumbar fibers through the inferior mesenteric and the hypogastric nerves which latter are also an afferent path from the bladder and pelvic organs. There is also a cranosacral supply through the pudendal nerve. Sympathetic activity causes a relaxation of the internal sphincter and rectum and, to a less extent, of the sigmoid and descending colon. Craniosacral impulses have an opposite effect. Thus the appearance of the colon is a good index of the balance between sympathetic and parasympathetic systems, a large colon representing sympathetic preponderance and a small one lowered sympathetic or increased craniosacral activity. The extrinsic control of the bowel is well shown in the results of sympathectomy in cases of megacolon, interruption of the sympathetic innervation producing a striking contraction in the diameter and length of the gut.

COLON TYPES

The size and position of the colon varies with the type of individual. A stocky, heavy-set male, with a small hypertonic stomach and perhaps a tendency to high blood pressure, will usually have a large redundant colon, all evidence of a relatively active sympathetic system. In contrast, we find the thin asthenic person, more commonly a woman, with a large atonic stomach and a short, narrow colon lying in the iliac fossa, showing a low blood pressure, with frequent complaints of colon discomfort, attacks of diarrhea, and the usual story of an irritable colon.

These are the hyposympathetics, and perhaps adrenal cortex is what they need. The emotional element is strong and often based upon a background of fear, social or family conflicts, or even a sudden drop in the Dow Jones averages. Men seem to manifest nervous strain and exhaustion at the pylorus, women in their colons. "Old maids" of both sexes are apt to be constipated.

There is a definite reciprocal relation between the behavior of the ascending and the lower descending portions of the colon. We are all familiar with the great dilatation of the cecum which occurs in obstruction of the descending segment, and some recent studies in Chicago have shown that an increase of tone in the descending colon causes a direct relaxation of the ascending portion. Peristalsis in the ascending colon is often accompanied by shortening of the distal segments. The ascending colon appears to be a dehydrator and the site of bacterial and cellulose digestion. The transverse and descending portions accomplish additional dehydration and gradual onward propulsion of their contents.

HOW NORMAL COLONS VARY FROM DAY TO DAY

In following individual normal colons day after day, we have been impressed by the variability of the same colon in tone and motility and the influence of an adequate water intake. An ample supply of water in persons not accustomed to it means quicker evacuation of the cecum and a less tonic descending portion. It is interesting that in several of the female patients there was a striking evacuation of the transverse and descending colon beginning two days before the onset of menstruation. Doctor Stone at the University of California Hospital has recently demonstrated changes in the length and size of the colon by refilling the bowel after a first enema has been expelled. Dilated loops are found narrower and shorter and the whole tone of the gut is often increased at least temporarily.

X-RAY EVIDENCE OF COLON IRRITABILITY

The x-ray evidence of colon irritability is found in hypertonicity of the transverse and descending colon; in broad, deep and widely spaced haustral constrictions or a comparative absence of haustra. Occasionally in acute cases we see fine, closely spaced constrictions of unequal depth which prob-

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